

**REMARKS**

Claims 9, and 17-20 are canceled without prejudice or disclaimer. Claims 1, 4, 10, 12,13, 14 and 15 are amended. Claims 21 and 22 are added, and are supported by original claims 4 and 10, respectively.

Claim 1 was amended to include the recitation of claim 9 by restricting the claim to thermostable mismatch repair protein(s). In addition the steps of denaturing and subsequently annealing the template polynucleotides were restricted to doing so by increasing and lowering the temperature, respectively, as recited in claims 12 and 13 respectively. Claim 1 was further amended to recite at least one repeat of steps (a) through (d). Claims 12 and 13 were amended according to claim 1. Claims 4 and 10 were amended in response to the rejections of the Office, as discussed below. Claims 14 and 15 were amended to provided proper antecedent basis.

The title of the invention has been amended to more accurately define the claimed invention, as requested by the Examiner.

It is respectfully submitted that the present amendment presents no new issues or new matter and places this case in condition for allowance. Reconsideration of the application in view of the above amendments and the following remarks is requested.

**I. The Title of the Invention**

A new title was requested that is clearly indicative of the invention to which the claims are directed. The title is amended herewith. Applicants respectfully request reconsideration and withdrawal of the objection.

**II. The Rejection of Claims 4, 10, 12, and 13 under 35 U.S.C. 112**

Claims 4, 10, 12, and 13 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite because of the term "preferably" in the claims. The claims presented herewith have been amended to remove the term "preferably".

For the foregoing reasons, Applicants submit that the claims overcome this rejection under 35 U.S.C. 112. Applicants respectfully request reconsideration and withdrawal of the rejection.

**III. The Rejection of Claims 10 and 11 under 35 U.S.C. 112**

Claims 10 and 11 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite because of the term "the thermostable mismatch repair protein(s)" lacks proper antecedent basis in claim 1. Since claim 1 has now been amended to recite the term "thermostable mismatch repair

protein(s)" (previously found in claim 9), this claim now provides antecedent basis for the term in claims 10 and 11.

For the foregoing reasons, Applicants submit that the claims overcome this rejection under 35 U.S.C. 112. Applicants respectfully request reconsideration and withdrawal of the rejection.

#### **IV. The Rejection of Claims 17 and 18 under 35 U.S.C. 112**

Claims 17 and 18 are rejected under 35 U.S.C. 112, first paragraph, for failing to comply with the written description requirement, because the claims are asserted to be "reach-through" product-by-process claims. Claims 17 and 18 have been canceled without prejudice or disclaimer.

This rejection is hereby rendered moot, and Applicants respectfully request withdrawal of the rejection.

#### **V. The Rejection of Claims 1-18 under 35 U.S.C. 102**

Claims 1-18 are rejected under 35 U.S.C. 102(b) as being anticipated by WO 99/29902. This rejection is respectfully traversed.

The presently claimed invention relates to methods for forming a plurality of recombined homologous double-stranded polynucleotides from at least two homologous double-stranded template polynucleotides. The method of the invention comprises a step of providing a solution of at least two non-methylated homologous double-stranded template polynucleotides, and one or more thermostable mismatch repair protein(s). The double-stranded template polynucleotides are then denatured by increasing the temperature, and subsequently annealed again by lowering the temperature, whereby heteroduplexes are formed. Then the thermostable mismatch repair protein(s) are allowed to repair the mismatches, thereby forming recombined new duplexes in the process. Finally, the whole process is repeated at least once, wherein the newly formed duplexes serve as new template polynucleotides in each repetition.

WO 99/29902 does not disclose the use of thermostable mismatch repair protein(s), nor does it disclose any advantages of using such thermostable proteins in a method that comprises steps of repeated heating and cooling, as claimed in the instant invention.

For the foregoing reasons, Applicants submit that the claims overcome this rejection under 35 U.S.C. 102. Applicants respectfully request reconsideration and withdrawal of the rejection.

**VI. The Rejection of Claim 1 under 35 U.S.C. 102**

Claim 1 is rejected under 35 U.S.C. 102(b) as being anticipated by Resnick et al. (US 5,334,522). This rejection is respectfully traversed.

Resnick et al. discloses *in vitro* hybridization of variant polynucleotides, whereby heteroduplex molecules are generated, and subsequent transformation of the generated heteroduplexes into various appropriate host cells for *in vivo mismatch repair* to take place, e.g., in *E. coli* mutants capable of localized repair of mismatches (See column 4, lines 60-68).

In contrast, the present invention relies on a wholly *in vitro* procedure, where a solution comprising at least two non-methylated homologous double-stranded template polynucleotides and one or more mismatch repair protein(s) is provided; the homologues are denatured and reannealed to form heteroduplexes; and then the mismatch repair protein(s) repair nucleotide mismatches in the heteroduplexes, wherein recombined new duplexes are formed.

For the foregoing reasons, Applicants submit that the claims overcome this rejection under 35 U.S.C. 102. Applicants respectfully request reconsideration and withdrawal of the rejection.

**VII. Conclusion**

In view of the above, it is respectfully submitted that all claims are in condition for allowance. Early action to that end is respectfully requested. The Examiner is hereby invited to contact the undersigned by telephone if there are any questions concerning this amendment or application.

Respectfully submitted,

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